Journal of Organometallic Chemistry, 260 (1984) 255–262
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

ALLYLSTANNATION

V *. *cis*-STEREOCONVERGENT SYNTHESIS OF HOMOALLYLIC ALCOHOLS AND 4-CHLORO-2,6-DIALKYL-3-METHYLTETRAHYDROPYRANS BY THE ADDITION REACTION OF 1-BUTEN-3-YLDICHLORO-n-BUTYLTIN AND ALDEHYDES

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(Received August 19th, 1983)

Summary

1-Buten-3-yl-n-butyldichlorotin, generated *in situ* by redistribution of (*E*/*Z*)-2-butenyltri-n-butyltin and $BuSnCl_3$, reacts readily with neat RCHO (R = CH_3, C_2H_5, $(CH_3)_2CH$) at 25°C to give linear alcohols $RCH(OH)CH_2CH{=}CHCH_3$ and/or 2,3,4,6-tetrasubstituted tetrahydropyrans, $\overline{CH_2CH(R)OCH(R)CH(CH_3)CH}$-(Cl), which are mainly in the *cis*-configuration with respect to the $CH(CH_3)$–CH(Cl) bond. When R = $(CH_3)_3C$ and C_6H_5, only the homoallylic alcohols are obtained.

These *cis*-stereoconvergent syntheses are explained in terms of kinetic control of the formation of adducts obtained by insertion of one or two aldehyde molecules into the organotin substrate.

Introduction

In recent years allyltins have assumed an important role among the family of allylic organometallics [1,2] used in stereocontrolled syntheses of open-chain compounds [3]. Crotyltributyltin adds stereospecifically to PhCHO at 200°C and to CCl_3CHO at 20°C [4] and stereoselectively to PhCHO in the presence of $BF_3 \cdot OEt_2$ [5]. A total *cis*-convergence ** is noted with the use of the ternary system (*E*/*Z*)-

* Ref. 9 is considered Part IV; for Part III see ref. 8.

** Stereoconvergence denotes the predominant formation of one and the same product stereoisomer from both stereoisomeric precursors (see ref. 2).

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$Bu_3SnCH_2CH{=}CHCH_3/RCHO/Bu_2SnCl_2$, where RCHO is a saturated [6] or an α,β-unsaturated aldehyde [7].

More recently 2-butenylbutyldichlorotin has been shown to be a very versatile reagent: this substrate reacts with aldehydes to form homoallylic alcohols and/or a mixture of *cis/trans*-4-chlorotetrahydropyrans, $CH_2CH(R)OCH(R)CH(CH_3)CH$-(Cl), in which the *trans*-isomer * is the major product [8]. Tetrahydropyrans are also formed by treatment of $X_3SnCH_2CH{=}CH_2$ compounds (X = Cl or Br) with C_2H_5CHO [9].

These reactions have been explained by using pathways in which the insertion of two aldehyde molecules into $BuCl_2SnCH_2CH{=}CHCH_3$ gives tin alkoxides of the type: $BuCl_2SnOCH(R)OCH(R)CHR'CH{=}CH_2$ (R' = H or CH_3), which collapse intramolecularly to the heterocyclic compounds.

In view of these findings, we have undertaken a study of the addition of $BuCl_2SnCH(CH_3)CH{=}CH_2$, generated *in situ* by redistribution of (*E/Z*)-$Bu_3SnCH_2CH{=}CHCH_3$ and $BuSnCl_3$, to aldehydes, RCHO (R = CH_3, C_2H_5, $(CH_3)_2CH$, $(CH_3)_3C$ and C_6H_5). Since α-methylallyltin substrates are known to give *cis*-stereocontrolled syntheses [6,7,10], we expected to find a *cis*-convergent control in the formation of the products.

Experimental

Details of the IR and NMR equipment and the preparation of the starting materials have been described previously [6,8].

GLC analyses were made with a Sigma-3P Perkin–Elmer apparatus operating with a flame-ionization detector.

Addition reactions

The procedures were as follows: (a) Equimolecular amounts (25 mmol) of (*E/Z*)-$Bu_3SnCH_2CH{=}CHCH_3$ (with various isomer ratios in the range 33/66 to 75/25) and RCHO were mixed. The mixture was added as quickly as possible to sufficient liquid $BuSnCl_3$ at 0°C in order to give a mol ratio Bu_3SnCH_2-$CH{=}CHCH_3/RCHO/BuSnCl_3$ of 1/1/1. Then the solvent-free mixture was allowed to reach a constant temperature at 25°C, under stirring. The progress of the reactions was monitored by infrared spectroscopy, as described previously [7,8]. Then, at the appropriate time, aqueous Na_2CO_3 2 *M* (15–20 ml) was added and the products extracted with ethyl ether. Volatile components were separated from the solid residues by trap-to-trap distillation in a cold bath (liquid nitrogen). The solvent was taken off by subsequent distillation.

Runs performed by this procedure are listed in Table 1. Three main products were obtained: linear and branched alcohols and 4-chloro-2,6-dialkyl-3-methyltetrahydropyrans (alkyl = C_2H_5, i-C_3H_7). 1-Buten-3-ol was also recovered in small quantities (cf. runs 1–3 of Table 1).

(b) Following procedure (a), runs were also performed in CH_2Cl_2 (30–40 ml). Results are given in Table 2.

(c) Another set of runs was performed using different molar ratios of the three

* The isomerism occurs at the $CH(CH_3)$–CH(Cl) bond.

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TABLE 1

RESULTS OF THE REACTIONS OF (*E*/*Z*)-2-BUTENYLTRI-n-BUTYLTIN WITH ALDEHYDES IN THE PRESENCE OF $BuSnCl_3$ AND ABSENCE OF SOLVENT ($Bu_3SnCrot/BuSnCl_3/RCHO = 1/1/1$)

Run no	RCHO R (mmol)	$Bu_3SnCH_2CH{=}CHCH_3$ *E*/*Z* ratio	Product (Amount) (g) Yield (%) [a]	Composition of the product mixture							
				Alcohols						4-Chloro-tetrahydro-pyran ($X_3 \times 100$) [b]		$CH_3CH(OH)CH{=}CH_2$ ($X_4 \times 100$) [b]
				Linear ($X_1 \times 100$) [b]		Branched ($X_2 \times 100$) [b]						
						threo		*erythro*		*trans*	*cis*	
				E	*Z*							
1	C_2H_5 (25)	33/66	2.5	54		9				32		5
			73	30	70	37		63		36	64	
2	C_2H_5 (35)	33/66	3.4	45		7				41		7
			68	30	70	43		57		22	78	
3	C_2H_5 (25)	33/66	2.4	50		6				42		2
			66	23	77	48		52		20	80	
4	$(CH_3)_2CH$ (25)	33/66	3.1	16		26				58		0
			75	0	100	59		41		15	85	
5	$(CH_3)_2CH$ (25)	57/43	2.95	9		37				54		0
			73	0	100	57		43		14	86	
6	$(CH_3)_2CH$ (25)	61/39	3.0	25		38				37		0
			79	0	100	63		37		13	87	
7	$(CH_3)_3C$ (25)	33/66	1.9	85		15				0		0
			53	0	100	12		88				
8	$(CH_3)_3C$ (25)	57/43	2.1	96		4				0		0
			59	0	100	0		100				
9	C_6H_5 (25)	33/66	2.3	66		33				0		0
			57	0	100	33		66				

[a] The total yield is based on the quantity of the tin substrate taken. [b] X_1, X_2, X_3, X_4 represent the mol fraction of the components.

TABLE 2

REACTIONS OF THE SYSTEM (*E*/*Z*)-2-BUTENYLTRI-n-BUTYLTIN/RCHO/$BuSnCl_3$ IN THE RATIO 1/1/1 IN CH_2Cl_2

Run no	RCHO R (mmol)	$Bu_3SnCH_2CH{=}CHCH_3$ *E*/*Z* ratio	Product (Amount) (g) Yield (%) [a]	Composition of the product mixture					
				Alcohols				4-Chloro-tetrahydro-pyran ($X_3 \times 100$) [b]	$CH_3CH(OH)CH{=}CH_2$ ($X_4 \times 100$) [b]
				Linear ($X_1 \times 100$) [b]		Branched ($X_2 \times 100$) [b]			
				E	*Z*	*threo*	*erythro*	*trans* *cis*	
10	C_2H_5 (25)	57/43	2.6	83		16		0	0
			91	0	100	48	52		
11	C_2H_5 (25)	66/33	2.7	87		13		0	0
			94	4	96	48	52		
12	$(CH_3)_2CH$ (25)	61/39	2.9	56		40		2.5	1.5
			89	0	100	66	34		

[a] and [b] as in Table 1.

TABLE 3

REACTIONS OF THE SYSTEM (*E*/*Z*)-2-BUTENYLTRI-n-BUTYLTIN/RCHO/$BuSnCl_3$ IN VARIOUS RATIOS 1/X/1 (X = 2.5–7)

Run no	RCHO R	$Bu_3SnCH_2CH{=}CHCH_3$ *E*/*Z* ratio (Amount (mmol))	$Bu_3SnCrot$/RCHO/$BuSnCl_3$ Mol ratio	Product (Amount) (g) Yield (%) [a]	Composition of the product mixture						
					Alcohols				4-Chloro-tetrahydro-pyran ($X_3 \times 100$) [b]		Trimeric aldehyde $(RCHO)_3$ ($X_4 \times 100$) [b]
					Linear ($X_1 \times 100$) [b]		Branched ($X_2 \times 100$) [b]				
					E	*Z*	*threo*	*erythro*	*trans*	*cis*	
13	CH_3	64/36 (30)	1/3.5/1	4.0	20		0		76		4
				86	Traces	~100			14	86	
14	CH_3	64/36 (30)	1/6/1	4.3	22		0		32		4.5
				43	14	86			12	88	
15	C_2H_5	75/25 (25)	1/2.5/1	2.6	12		0		85		3
				78	20	80			18	82	
16	C_2H_5	57/43 (25)	1/3.5/1	4.3	11		0		82		7
				98	18	82			12	86	
17	C_2H_5	66/33 (25)	1/4/1	4.0	24		0		68		8
				91	Traces	~100			12	88	
18	C_2H_5	66/33 (25)	1/5/1	4.5	19		0		62		19
				90	Traces	~100			10	90	
19	C_2H_5	75/25 (25)	1/7/1	3.8	16		0		31		53
				45	11	89			10	90	
20	$(CH_3)_2CH$	61/39 (25)	1/6/1	4.2	52		0		33		15
				90	0	100			16	84	

[a] and [b] as in Table 1.

components, $Bu_3SnCH_2CH{=}CHCH_3/RCHO/BuSnCl_3$, ranging from 1/2.5/1 to 1/7/1 (Cf. Table 3).

Characterization of the compounds obtained and analysis of the recovered mixtures were made by ^{13}C NMR and IR spectroscopy, mass spectra and GLC analysis as described previously [8]. For quantitative determinations the ^{13}C NMR spectra were recorded using sufficiently long pulse intervals to avoid saturation of the nuclear spins (at least 25 s) and the nuclear Overhauser effect (NOE) was suppressed by the gated decoupling method [11].

Results and discussion

For all of the systems studied here, allylstannation takes place under mild conditions: reaction is complete in less than 1 h when $R = CH_3$, C_2H_5 or $i\text{-}C_3H_7$, in 24 h when $R = C_6H_5$ and in 2 days when $R = (CH_3)_3C$.

4-Chloro-2,6-dialkyl-3-methyltetrahydropyrans ($R = CH_3$, C_2H_5 and $i\text{-}C_3H_7$), predominantly in the *cis*-isomeric form, were obtained, together with homoallylic alcohols, by mixing equimolecular amounts of the three components, $Bu_3SnCH_2CH{=}CHCH_3/RCHO/BuSnCl_3$ (cf. Table 1). Under the same conditions only the carbinols were recovered when $R = C_6H_5$ and $(CH_3)_3C$.

In CH_2Cl_2 solution, still operating with equimolecular amounts of the three reagents (cf. Table 2), only carbinols were obtained.

The formation of chlorotetrahydropyrans is predominant (cf. Table 3) when the reaction is carried out with an excess of aldehyde. Figure 1 describes, as an example, the behaviour of the system with C_2H_5CHO; it gathers together the findings of runs 1–3 of Table 1 and runs 15–19 of Table 3. The yield of the chlorotetrahydropyran increases to reach a maximum value (82–85%) for a mol ratio $C_2H_5CHO/Bu_3SnCrotyl$ in the range 2–3; then, for higher mol ratio values, it decreases because

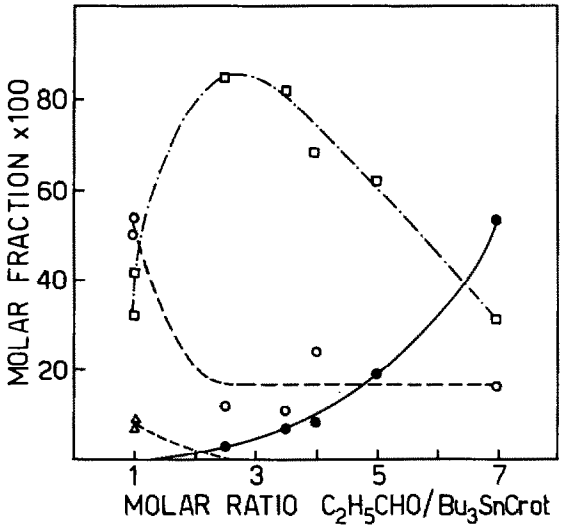
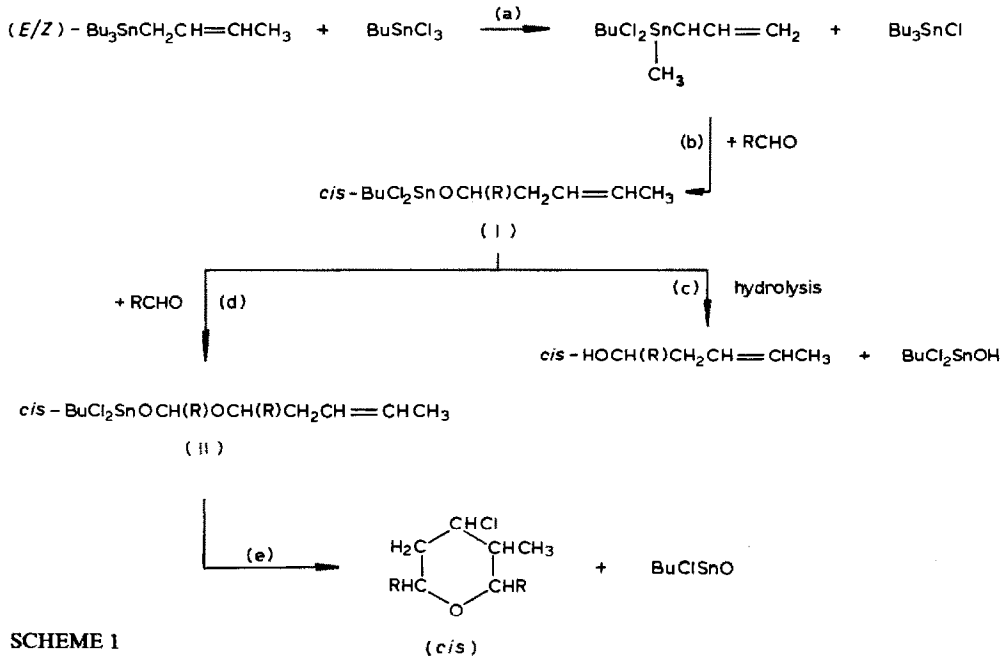


Fig. 1. Dependence of the product composition on the $C_2H_5CHO/Bu_3SnCH_2CH{=}CHCH_3$ mol ratio, in absence of solvent: runs 1–3 and 16–19 (cf. Tables 1 and 3). 4-Chloro-2,6-diethyl-3-methyltetrahydropyran (□), linear alcohols (○), branched alcohols (△), trimeric aldehyde $(C_2H_5CHO)_3$ (●).

of the competitive reaction leading to the trimeric aldehyde (compare with ref. 8).

The most striking feature of these results is the high *cis*-convergence in the formation of both linear homoallylic alcohols and chlorotetrahydropyrans. Both of these compounds arise from addition reactions shown in Scheme 1.

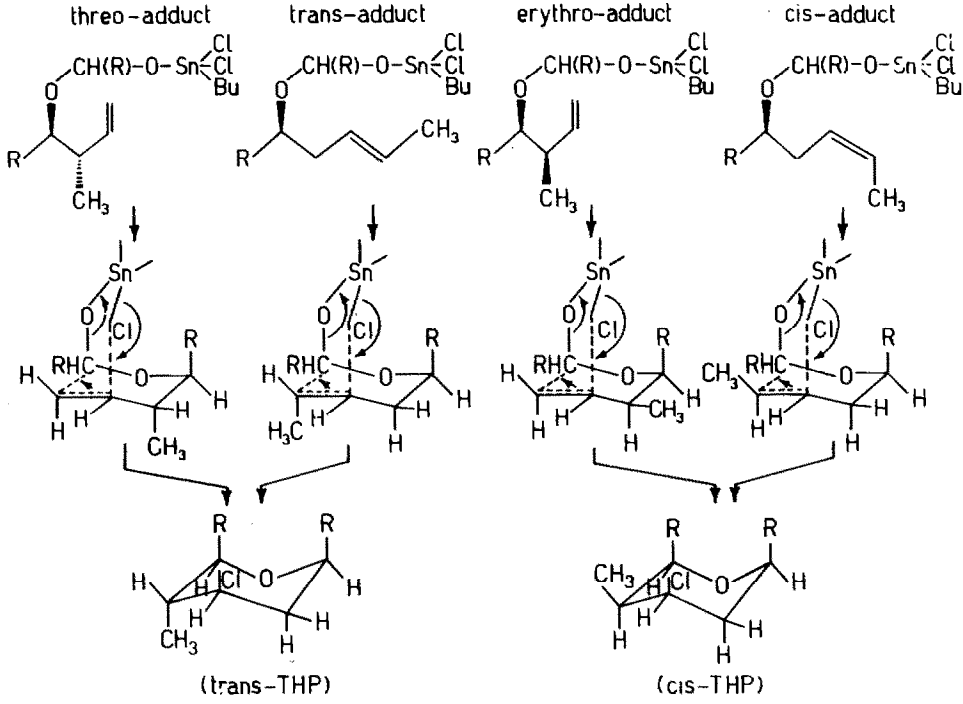


SCHEME 1

Step a represents the fast redistribution process giving the α-methylallyltin substrate. Adduct I, formed by the addition step b, is expected to have a *cis*-configuration both on the basis of previous arguments [6] and because α-methylallyltins have been found [6,7,10] to give rise to kinetically-controlled reactions leading to products with the *cis*-configuration. Hydrolysis of I leads to linear homoallylic alcohols completely in the *cis*-configuration (step c), whereas the further insertion of an aldehyde molecule into the Sn–O bond of I (step d) allows the formation of adduct II which maintains the same linear *cis*-configuration. The intramolecular rearrangement of II (step e) is still a stereocontrolled reaction giving stereospecifically the chlorotetrahydropyran in the isomeric form with the *cis*-configuration.

The present results, together with those dealing with the systems $BuCl_2SnCH_2$-$CH{=}CHCH_3$/RCHO [8] in which a *trans*-convergence in the formation of the chlorotetrahydropyrans was found, permit us to put forward a general view of the stereospecific formation of *cis*- and *trans*-chlorotetrahydropyrans as depicted in Scheme 2.

Crotyl- and α-methylallyltin substrates can form, with aldehydes, the four isomeric adducts: *threo, trans, erythro* and *cis*. Their rearrangements, probably through transition states with bicyclononane structures, as shown in the scheme, give rise stereospecifically to *trans*- or *cis*-chlorotetrahydropyrans. In the present case it is probable that the *cis*-adduct is formed preferentially, so that the final products are predominantly *cis*. The recovery from some experiments of small amounts of *trans*-chlorotetrahydropyrans (0–20%) is attributed to some isomerization of the



SCHEME 2

α-methylallyltin substrate in the presence of $BuSnCl_3$, leading crotyltin isomers. These are known [8] to form *threo* and *erythro* adducts with aldehydes, which lead eventually to *trans* and *cis* products, respectively.

Acknowledgements

We thank Prof. Douglas P. Graddon (University of Sidney, Australia) who accepted the task of improving the English text and of looking it over critically.

The financial support by CNR (Rome) under the "Progetto Finalizzato del CNR per la Chimica Fine e Secondaria" is acknowledged.

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